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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,280	09/26/2003	Gregory Alan Lazar	067461-5121US	8317

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EXAMINER	
DAHLE, CHUN WU	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
04/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,280	LAZAR ET AL.	
	Examiner	Art Unit	
	CHUN DAHLE	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/04/2008, 01/04/2009, and 02/17/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88-92,94-112,135-137 and 139-144* is/are pending in the application.

4a) Of the above claim(s) *90-92,94-102,107,110,141 and 143* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88, 89, 103-106, 108, 109, 111, 112, 135-137, 139, 140, 142, and 144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments to the claims, filed on August 4, 2008, August 5, 2008, January 14, 2009, and February 17, 2009, are acknowledged.

Claims 1-87, 93, 113-134, and 138 have been canceled.
Claims 139-144 have been added.

Claims 88-92, 94-112, 135-137, and 139-144 are pending.

Applicant's argues that the species of additional positions of the Fc region should be examined together with the elected position 239D because applicant believe that 239D is free of the prior art (see Remarks filed on August 4, 2008). This is not found persuasive because the elected species 239D has been rejected for reasons of record. Because no generic claim was found allowable, the prior art search will not be extended unnecessarily to cover all nonelected species of other positions in the Fc region at this time. *Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.* See Office Action, mailed on February 7, 2008 for detail discussion.

Upon further consideration, the prior art search has been extended to cover additional species of 239E, 239Q, and 239T that have enhanced binding affinity to an FcγR.

Claims 90-92, 94-102, 107, 110, 141, and 143 have been withdrawn from further consideration under 37 C.F.R. 1.142(b) as being drawn to nonelected inventions.

Claims 88, 89, 103-106, 108, 109, 111, 112, 135-137, and newly added claims 139, 140, 142, and 144 are currently under consideration only to the extend as they read on the originally elected invention of Group I and species of IgG1, targeting CD20 antigen, 239D, 239E, 239Q, and 239T with enhanced binding affinity to an an FcγR, with no engineered glycoforms.

2. This Office Action is in response to Applicant's amendment to the claims and remarks filed on August 4, 2008, August 5, 2008, January 14, 2009, and February 17, 2009.

The rejections of record can be found in the previous Office Actions, mailed February 7, 2005 and October 21, 2005.

3. Upon further consideration, it appears that the priority application USSN 60/414,433 provides support for 239D and 239E.

4. The references US 2008/0071063, US 2007/0087005, and WO 05102387 cited in applicant's arguments under "Secondary Indicia of Non-Obviousness" on page 13 of the Remarks (filed on January 14, 2009) have been listed on PTO-892. Copy of WO 05102387 has been provided herein.

5. In view of applicant's amendment to the claims, the prior rejection under 35 U.S.C. 112, first paragraph, enablement, has been withdrawn.

6. In view of applicant's amendment to the claims, the prior rejection under 35 U.S.C. 112, first paragraph, written description, has been withdrawn.

7. In view of applicant's amendment to the claims, the prior rejection under 35 U.S.C. 102(e), has been withdrawn.

8. Claim 112 is objected to for following informality:

Claim 112 appears to have a typographical error of "any of claims 88-9392". Appropriate correction is required. For examination purposes, claim 112 is read as dependent upon claim 88.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 88, 89, 103-106, 108, 109, 111, 112, 135-137, and newly added claims 139, 140, 142, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Presta (US Patent 6,737,056. Reference A97 on IDS) for reasons of record.

Applicant's arguments in conjunction with the various legal citations, filed on August 4, 2008, and January 14, 2009, have been fully considered but have not been found persuasive.

Applicant's arguments relying upon Ex Parte Watkins, filed on August 4, 2008, is acknowledged. Such arguments are rendered moot for following reasons:

A) the opinion of *Ex parte Watkins* has not been designated as precedential opinion and each application must be examined on its own merits.

B) The *Ex parte Watkins* deals with rejection under 35 U.S.C. 102(e), while the current rejection is under 35 U.S.C. 103(a). Thus, the analysis in *Ex parte Watkins* would not be applicable here.

C) the prosecution for USSN 10/370,749 (the application in *Ex parte Watkins*) has been reopened and new ground of rejection under 35 U.S.C. 103(a) has been added. The case has since been abandoned.

Applicant argues that the claims in Presta's patent 6,737,056 are allowed because of the Examiner's error.

This is argument regarding the validity of the claims in the US Patent is rendered moot for following reasons:

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims. See 35 U.S.C. 282. In addition, the question of validity or invalidity is exclusively a matter to be determined by a court. See MPEP 1701.

Further, applicant argues that Presta dose not teach substitutions in position 239 for increased binding affinity to an FcγR. Applicant asserts that Presta's teachings are only limited to S239A with decreased binding to FcγRs. Applicant argues that Presta is not an enabling prior art and there is inadequate written description regarding substitution in position 239 for increased binding to FcγRs. Applicant argues that the prior art teach S239A substitution with decreased binging to FcγRs; such teaching would not lead one of skill in the art to make 239D, 239E, 239Q, 239T for increased binding for FcγRs. Applicant argues that Alanine is hydrophobic but the claimed D, E, Q, and T are acidic. Applicant asserts that different amino acid substitutions in the same position would yield opposite effect of the binding to FcγRs.

This is not found persuasive for following reasons:

The Presta's teaches that the Fc region of an antibody or an immunoadhesin can be altered so that the Fc-related effector functions of the antibody or immunoadhesin can be changed. The scope of the prior art embodiment is not simply limited to what amino acid residues to use to substitute a given pre-existing residue. The key invention of Presta is the identifications of positions, e.g. 239 in the Fc region, that interact with the Fc gamma receptors. Presta teaches that S239 is involved in binding of the FcγRs (e.g. see column 3).

In contrast to applicant's reliance on the working examples and preferred embodiments of the prior art, it is noted that Presta provides guidance regarding amino acid substitutions using different naturally occurring residues. For example, Presta teaches that in addition to Ala (A), the preexisting residues in positions involved in FcγR binding (e.g. S239) can be substituted with any other amino acid residues (e.g. see last paragraph on column 19). Presta teaches that pre-existing neutral hydrophilic residues such as Ser (S) can be conservatively substituted with residues from the same group e.g. Thr (T) (e.g. see Table 1 on column 20). Further, Presta teaches non-conservative substitutions involving the use of amino acid residue with significant different side chain properties; for example, for Ser (belongs to neutral hydrophilic group) one can use Asp (D) or Glu (E) (both belong to acidic group) or Gln (Q) (basic group) for non-conservative substitutions that would result in substantial modifications in the biological properties of the Fc region. As stated previously, the position 239 of the Fc region taught by Presta provides a point of intervention for altering the efffector function of an antibody. Presta's teaching is enabling in the sense that it allows one of ordinary artisan to make Fc variants with S239 substituted to any other naturally occurring residues and to select the Fc variants with increased affinity to FcγRs. A person of ordinary skill has good reason to pursue the known options, e.g. making S239D (see column 12 and paragraphs between Tables in column 20 of Presta), within his or her technical grasp with reasonable expectation of success.

Therefore, making conservative substitution S239T, or non-conservative substitutions S239D, S239E and S239Q and testing for the variants' binding affinity for FcγRs does not require a leap of inventiveness

The Examiner agrees with applicant's assertions that the twenty natural occurring amino acids have very different chemical characteristics. This is true based upon the teachings of Presta. Thus, one of skill in the art would not be discouraged from testing more amino acid residues in position 239 even if Presta's working example S239A shows decreased binding to FcγR because position 239 is involved in binding to its receptors and substitution made in 239 clearly alters the binding affinity to FcγRs. A person of ordinary skill has good reason to pursue the known options (e.g. amino acid substitutions at position 239 of the Fc region) within his or her technical grasp. Even if the twenty amino acid residues cannot simply substituted one for another, such unpredictability could not be equated with nonobviousness here because there were only a finite number of naturally occurring amino acid residues (nineteen, excluding the preexisting residues) to be tested in position 239 for altered affinity to the FcγRs. A person of ordinary skill in the art would have had a reasonable expectation that 239 variants within the claimed scope could have been successfully obtained.

Thus, the claimed S239D, S239E, S239Q, and S239T are simply predictable variations.

In addition, applicant argues that the claims are non-obvious over Presta because of the commercial success of the 239 variants by a number of companies.

This is not found persuasive for following reasons:

In contrast to applicant's assertion, it is noted that no objective evidence of commercial success has been provided. Further, there is a lack of establishment with regard to a nexus between the claimed invention and the evidence of commercial success. Applicant's mere assertion of commercial success does not establish a nexus between the claimed invention and the commercial success because there is no evidence that the product has been sold and that said

product corresponds to the claimed invention or whatever commercial success may have occurred is attributable to the antibody or immunoadhesin defined by the claims. See MPEP 716.03.

Therefore, applicant's arguments have not been found persuasive.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 88, 89, 103-106, 108, 109, 111, 112, 135-137, 139, 140, 142, and 144 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the following copending applications for reasons of record:

claims 1, 2, 10, 13, 17, and 18 of copending USSN11/124,620,
claims 9-12, and 19 of copending USSN 11/396,495,
claims 1-5, 7-13, 20, and 21 of copending USSN 11/538,406,
claims 1-5, 8-13, 15, 20, and 21 of copending USSN 11/538,411,
claims 1, 4-17, and 20-24 of copending USSN 11/544,165,
claims 1, 3, 5, 6, 9, and 11-13 of copending USSN 11/765,402,
claims 2, 13-17, and 38 of copending USSN 11/618,457,
claims 2, 13-17, and 38 of copending USSN 11/618,472,
claims 2, 13-17, and 38 of copending USSN 11/618,488,
claims 1, 3, 5, 6, 9, and 11-13 of copending USSN 11/764,001,
claims 1, 3, 5, 6, 9, and 11-13 of copending USSN 11/765,353,
claims 1, 3, 5, 6, 9, and 11-13 of copending USSN 11/765,390,
claims 1, 3, 5, 6, 9, and 11-13 of copending USSN 11/765,402,
claims 1, 3, 5, 6, 9, and 11-13 of copending USSN 11/766,609.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's amendments filed on August 4, 2008, August 5, 2008, January 14, 2009, and February 17, 2009; the rejections are maintained for the reasons of record

13. It is noted that applicant has a number of copending applications (at least forty-four) in the instant family of applications encompassing Fc variants (see LETTER TO EXAMINER AND STATEMENT OF RELATEDNESS filed on August 4, 2008).

Given the history of a number of continuations-in-part, it is not readily apparent whether the claims were subject to restriction and whether the claims are subject to double patenting rejections.

Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Conclusion: no claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Eileen O'Hara can be reached 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Dahle
Patent Examiner
April 10, 2009

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644